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Efficacy of dexamethasone in the prophylaxis of nausea and vomiting during the postoperative period of laparoscopic cholecystectomy☆

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A B S T R A C T

Objective: To verify the efficacy of dexamethasone in the prophylaxis of nausea and vomiting in patients submitted to laparoscopic cholecystectomy.
Methods: This was a systematic review of the literature through the MEDLINE, Embase, and LILACS databases. Only controlled and randomized clinical trials comparing dexamethasone to placebo in the prophylaxis of nausea and vomiting in patients submitted to laparoscopic cholecystectomy were included.
Results: The results of this review were based on data from 12 controlled and randomized clinical trials, totaling 947 patients. The group of patients who received preoperative dexamethasone showed lower incidence of nausea (number needed to treat [NNT] = 7), vomiting (NNT = 7), and need for smaller doses of rescue antiemetics (NNT = 6).
Conclusion: The preoperative infusion of 8 mg of dexamethasone decreases the risk of complications in the postoperative period for patients submitted to laparoscopic cholecystectomy.

Eficácia da dexametasona na profilaxia de náuseas e vômitos no pós-operatório de colecistectomia laparoscópica

Palavras-chave:
Colecistectomia laparoscópica
Colelitíase
Dexametasona
Náusea e vômito pós-operatório

R E S U M O

Objetivo: Verificar a eficácia da dexametasona na profilaxia de náuseas e vômitos em pacientes submetidos à colecistectomia laparoscópica.
Métodos: Revisão sistemática da literatura através das bases de dados MEDLINE, EMBASE e LILACS. Foram incluídos apenas ensaios clínicos controlados e randomizados que compararam a dexametasona ao placebo na profilaxia de náusea e vômito em pacientes submetidos à colecistectomia laparoscópica.

☆Study conducted at the Academic Center for Studies and Researches in Evidence-Based Medicine of Faculdade de Medicina, Centro Universitário Lusíada, Santos, SP, Brazil.

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Resultados: Os resultados desta revisão basearam-se em dados de 12 ensaios clínicos controlados e randomizados, totalizando 947 pacientes. O grupo de pacientes que recebeu dexametasona pré-operatória apresentou menor incidência de náusea (NNT = 7), de vômito (NNT = 7) e de necessidade de antieméticos de resgate (NNT = 6).
Conclusão: A infusão pré-operatória de 8 mg de dexametasona diminui o risco de complicações no pós-operatório de pacientes submetidos à colecistectomia laparoscópica.

Introduction

Laparoscopic cholecystectomy is one of the most frequently performed elective surgeries around the world. Despite the fact that it is a highly safe procedure, complications such as nausea, vomiting, and pain are frequent during the postoperative period, and are among the main causes of patient complaints and dissatisfaction.[1,2] The main risk factors for nausea and vomiting are female gender, non-smoking patients, and previous history of these problems.[3,4]

Dexamethasone, a corticosteroid, has well-defined antiemetic, anti-inflammatory, and analgesic effects, in addition to having few side effects when administered in small doses. It is widely used for controlling nausea and vomiting in chemotherapy patients.

The objective of this review was to verify the efficacy of dexamethasone in the prophylaxis of nausea and vomiting in patients submitted to laparoscopic cholecystectomy.

Methods

Selection criteria

Types of studies
Only controlled and randomized clinical trials (Phase III studies) that assessed the efficacy of dexamethasone in the prevention of postoperative complications in patients submitted to laparoscopic cholecystectomy were included.

Participants
Inclusion criteria were patients with benign pathologies of the bile ducts submitted to elective laparoscopic cholecystectomy. Exclusion criteria were patients with a history of preoperative nausea and vomiting, or chronic use of analgesics or corticosteroids.

Types of interventions
Patients who received a preoperative infusion of dexamethasone, regardless of the moment, were considered part of the intervention group. The control group was formed by patients who received a preoperative infusion of placebo. Studies that associated the corticosteroid to any antiemetic drugs during the preoperative period were excluded.

Types of outcomes
The analyzed outcomes were nausea, vomiting, need for antiemetic and analgesic drugs, postoperative complications, and length of hospital stay.

Search strategies

The MEDLINE, Embase, and LILACS electronic databases were queried until July 2012.

The MEDLINE database was queried through PubMed, using the following search strategy: (adrenal cortex hormones OR dexamethasone) AND (postoperative nausea and vomiting OR nausea OR vomiting) AND (laparoscopic cholecystectomy) AND (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract]) AND (controlled[Title/Abstract]) AND (trial[Title/Abstract]).

In Embase, the following strategy was used: (adrenal cortex hormones OR dexamethasone) AND (postoperative nausea and vomiting) AND (laparoscopic cholecystectomy) AND (randomized controlled trial).

In LILACS, the following strategy was used: ("Colecistectomia Laparoscópica") AND ("Glucocorticoides" OR "Corticoides") AND ("Náusea e Vômito Pós-Operatório" OR "Náusea" OR "Vômito").

A manual search was also conducted for references from the selected studies, in order to find studies that were not included in electronic searches.

Quality of the methodology

Quality of the primary studies was assessed through the criteria proposed by Jadad et al.,[5] which analyze the description of the randomization, adequacy of the randomization, description of the blinding, adequacy of the blinding, and description of loss to follow-up. Only studies with score higher than 3 were included in the comprehensive analysis of the review.

Statistical analysis

All data were analyzed based on the intention of treatment; patients were analyzed within the groups to which they were randomized, regardless of the treatment and protocol irregularities.

Effectiveness or harm measurements expressed in absolute numbers were analyzed through the absolute risk difference (Mantel-Haenszel), adopting a confidence interval of 95%. When there was a statistical difference between the groups, the number needed to treat (NNT) or the number needed to harm (NNH) was calculated.

Inconsistencies among the clinical trials were estimated through the Chi-squared test (χ^2) for heterogeneity, and quantified using the I^2 test. Values above 50% were deemed relevant.

A sensitivity analysis was performed, including only studies with type II error < 20%.

Results

Fifty six studies were retrieved through the search strategies in the three primary databases used. After reading all relevant titles and summaries, 15 articles potentially fit for inclusion in the review were selected.[6-20] Of these, three were excluded after a complete reading: the first was excluded because it had a Jadad score < 3 and also because it did not present sufficient data for the intention-to-treat analysis;[16] the second study, due to the lack of results in absolute terms;[10] the third study, for not being described as double-blind, in addition to the lack the of the total number of patients who presented the outcomes.[9] Thus, this review included data from 12 controlled and randomized clinical trials, amounting to 947 patients (471 in the dexamethasone group and 476 in the placebo group).

Of the included studies, 11[6,8,11-20] used an 8 mg intravenous dose of dexamethasone, while one[7] used 5 mg. The infusion time ranged from 90 minutes before the beginning of the surgery until the anesthesia.

Incidence of nausea and vomiting

The overall incidence of nausea during the postoperative period of patients submitted to laparoscopic cholecystectomy was 27.9%, of which 94 cases occurred in the dexamethasone group and 171 cases occurred in the placebo group. Patients who received corticosteroid during the preoperative period showed a reduction in the absolute risk of nausea by 16% (95% CI: 0.11 to 0.22; $p < 0.001$; $I^2 = 20\%$; NNT = 7) when compared to patients who received saline solution (Fig. 1).

For the incidence of vomiting, patients who received a dose of corticosteroid showed reduction in the risk by approximately 15% (12.3% x 27.5%; 95% CI: 0.10 to 0.20; $p < 0.001$; $I^2 = 0\%$; NNT = 7; Fig. 1).

Need for antiemetic medication

Seven primary studies analyzed the need for antiemetic medication in the postoperative period as an outcome.[7,8,11,13,17,19,20] Patients who received corticosteroid needed a smaller dose of rescue antiemetic, representing a reduction in the risk by approximately 18% (12.8% x 30.6%; 95% CI: 0.12 to 0.23; $p < 0.001$; $I^2 = 52\%$; NNT = 6) when compared to the placebo group (Fig. 1).

Removing from the analysis both studies that resulted in relative heterogeneity,[11,17] the same effect remained ($p < 0.001$; $I^2 = 0\%$; NNT = 6).

Sensitivity analysis

The sensitivity analysis was performed using the statistical power found in the primary studies regarding each outcome, pursuant to Table 1. Using this tool as a methodological criterion, it was verified that the only benefit found with the use of the preoperative corticosteroid was the reduction in the need for antiemetics (NNT = 4).

The study using a reduced dose of dexamethasone (5 mg)[7] did not change the comprehensive analysis of the review. However, when analyzed separately, no benefit regarding the reduction in nausea and vomiting was verified.

Discussion

Laparoscopic surgery drastically reduced the metabolic, hormonal, inflammatory, and immune responses related to surgical trauma, thus it has become the routine procedure for treatment of cholelithiasis. Nonetheless, a high incidence of nausea and vomiting, the main reasons for extended hospital stays, is reported in the postoperative period.[1,2]

Nausea and vomiting after a laparoscopic cholecystectomy are caused by multiple factors, depending especially on intra-abdominal manipulation and formation of pneumoperitoneum, which stretches the peritoneum and irritates the diaphragm and viscera.[7,8]

The mechanism by which glucocorticoids may alleviate such complications is not fully understood, but the effects are probably centrally mediated through inhibition of the prostaglandin synthesis and/or inhibition of the release of endogenous opioids, serotonergic inhibition in the gastrointestinal tract, and decrease in inflammation of the surgical site, reducing parasympathetic impulses to the area postrema.[21-23]

Using tools and careful analyses of both quality of the methodology and internal and external validity, this review showed, through compelling data, the decrease in the risk of nausea and vomiting related to the surgery. Factors that could potentially generate clinical heterogeneity among the studies were assessed. Regarding the population, the articles follow the clinical practice, with a predominance of women in the fourth and fifth decade of life with low

Table 1 – Statistical power established in each primary study.

Study	Incidence of nausea	Incidence of vomiting	Need for antiemetics
Alghanem SM et al., 2010	10.1%	31.8%	13.4%
Bianchin A et al., 2007	27.1%	42.5%	*
Bisgaard T et al., 2003	32.5%	51.9%	34.8%
Erhan Yet al., 2008	77.7%	18.1%	*
Feo CV et al., 2006	71.0%	71.0%	97.2%
Fujii Y et al., 2010	29.5%	41.3%	*
Fukami Y et al, 2009	50.3%	35.2%	*
Murphy GS et al., 2011	77.1%	17.9%	38.1%
Nesek-Adam V et al., 2007	54.3%	53.6%	46.6%
Sánchez-Rodriguez PE et al., 2010	*	*	94.3%
Wang JJ et al., 1999	45.4%	69.1%	*
Wang JJ et al., 2002	42.5%	35.9%	68.7%

*This outcome was not evaluated in the study.

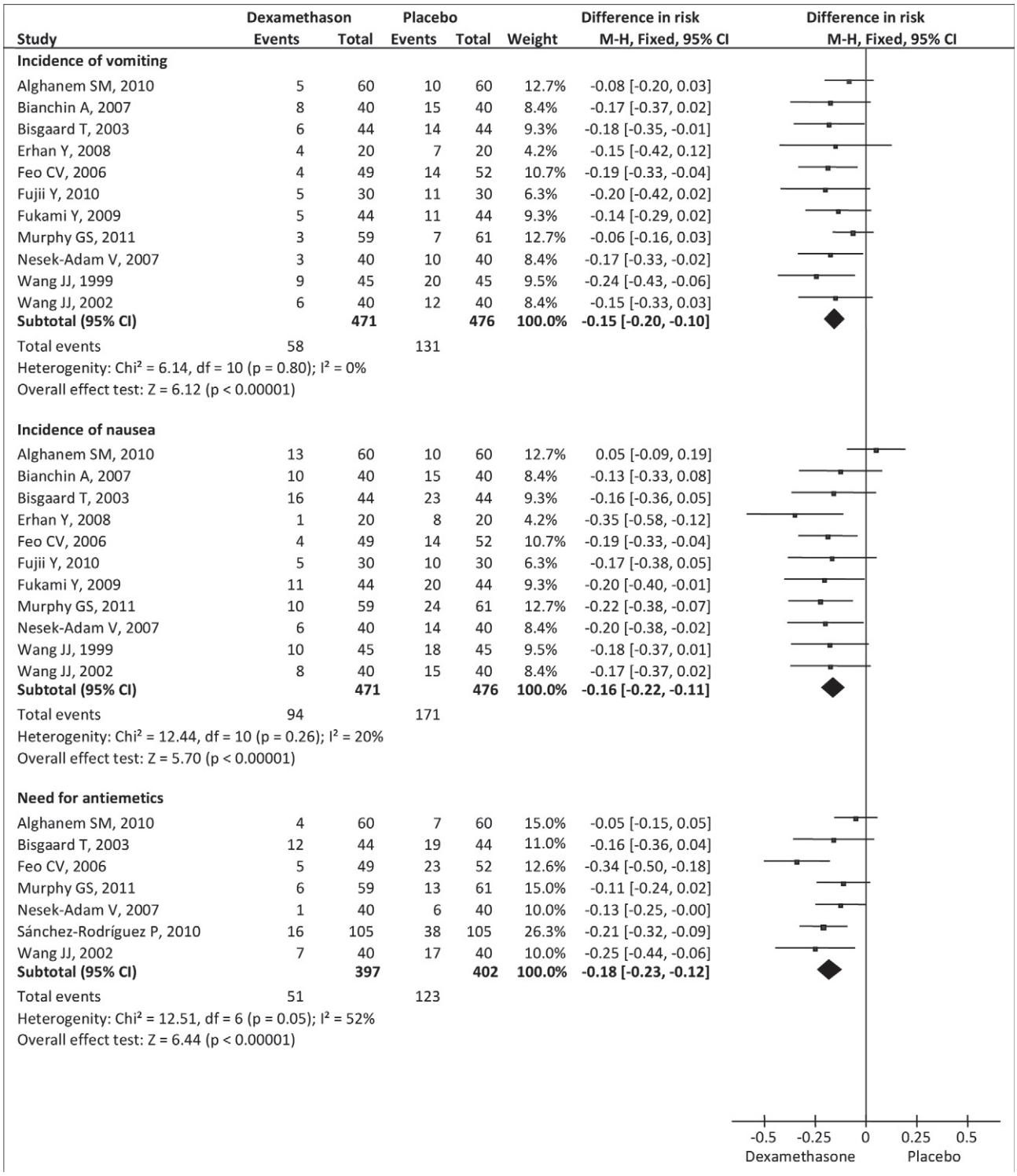

Fig. 1 – Meta-analysis on the efficacy of dexamethasone in the prophylaxis of postoperative complications in patients submitted to laparoscopic cholecystectomy. 95% CI, 95% confidence interval; F, female; M, male.

comorbidity index (ASA I-II). Regarding the intervention, the confounding factors were: 1) the duration of the surgery (approximately 1 hour), which did not present clinically significant differences among the studies; 2) the protocols of perioperative analgesia; 3) the moment of corticosteroid administration, which ranged from 90 minutes before the surgery until the anesthetic induction.

Despite the known risks of infection, impairment of the surgical wound healing, hyperglycemia, and adrenal insufficiency related to the use of corticosteroids, no study

reported an increase in the risk of adverse effects. Additionally, the use of dexamethasone is known to prevent the sedative, dysphoric, and extrapyramidal effects related to traditional drugs such as droperidol and metoclopramide.

Data obtained in this review may reinforce the idea of performing laparoscopic cholecystectomy as an ambulatory procedure, resulting in lower hospital costs, reduction in surgery waiting times, and less discomfort for the patient. Thus, surgeons and anesthetists should contemplate the prophylactic use of dexamethasone in patients submitted to laparoscopic cholecystectomy, especially in those more prone to nausea and vomiting.

Conclusion

The preoperative infusion of 8 mg of dexamethasone decreased the risk of complications in the postoperative period for patients submitted to laparoscopic cholecystectomy.

Conflicts of interest

The authors declare no conflicts of interest.

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